

AMENDMENTS TO THE CLAIMS

Claims 1 to 36. (Cancelled).

Claim 37. (Currently Amended) A method for first line treatment of type 2 diabetes, in a drug naïve human patient [[.]] who has had no previous oral hyperglycemic treatment or has had no oral hyperglycemic treatment for 2 months, which comprises administering to a drug naïve human patient in need of treatment, as first line therapy, a low dose of a combination of metformin and glyburide, where the glyburide has a particle size distribution so that at most [[10]] 25% of the particles of the glyburide are less than [[2]] 11 μm and at most [[10]] 25% of the particles of the glyburide are greater than [[60]] 46 μm, wherein the metformin in said low dose combination is administered in a daily dosage in an amount within the range from about 160 mg to about 750 mg, and the glyburide in said low dose combination is administered in a daily dosage in an amount within the range from about 0.5 to about 15 mg.

Claims 38 to 44. (Cancelled).

Claim 45. (Previously Presented) The method as defined in Claim 37 wherein the low dose combination of metformin and glyburide is formulated as a single dosage form.

Claim 46. (Previously Presented) The method as defined in Claim 37 wherein the metformin in said low dose combination is employed in a weight ratio to glyburide within the range from about 400:1 to about 50:1.

Claim 47. (Previously Presented) The method as defined in Claim 37 wherein the metformin and glyburide in said low dose combination are employed in a weight ratio to each other of about 200:1 or 100:1.

Claim 48. (Previously Presented) The method as defined in Claim 37 wherein the metformin in said low dose combination is administered in an amount within the range from about

160 to about 750 mg, one to four times daily, provided that the maximum daily dosage for metformin is about 750 mg per day, but more than about 225 mg, and the glyburide in said low dose combination is administered in an amount within the range from about 0.75 to about 5 mg, one to four times daily, up to a maximum of 15 mg per day.

Claim 49. (Previously Presented) The method as defined in Claim 37 wherein the metformin in said low dose combination is administered in an amount within the range from about 250 to about 500 mg, and the glyburide in said low dose combination is administered in an amount within the range from about 1.25 to about 5 mg.

Claim 50. (Previously Presented) The method as defined in Claim 37 wherein the combination of metformin and glyburide in said low dose combination comprises 250 mg metformin/1.25 mg glyburide.

Claim 51. (Previously Presented) The method as defined in Claim 37 wherein the combination of metformin and glyburide in said low dose combination comprises 500 mg metformin/2.5 mg glyburide.

Claim 52. (Previously Presented) The method as defined in Claim 37 wherein the combination of metformin and glyburide in said low dose combination comprises 500 mg metformin/5 mg glyburide.

Claim 53. (Previously Presented) The method as defined in Claim 37 wherein the combination of metformin and glyburide in said low dose combination comprises a 250 mg metformin/1.25 mg glyburide dosage administered once a day or twice a day.

Claim 54. (Previously Presented) The method as defined in Claim 53 wherein the 250 mg metformin/1.25 mg glyburide dosage is administered to a patient with a baseline hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) > 9% or a fasting glucose > 200 mg/dL twice daily, with dosage increases, where necessary,

in increments of 250 mg metformin/1.25 mg glyburide every 2 weeks, up to the minimum effective daily dose necessary to achieve adequate glycemic control.

Claims 55 to 57. (Cancelled).

Claim 58. (Currently Amended) A method for first line treatment of type 2 diabetes, in a drug naïve human patient~~[[,]]~~ who has had no previous oral hyperglycemic treatment or has had no oral hyperglycemic treatment for 2 months, which comprises administering to a drug naïve human patient in need of treatment, as first line therapy, a low dose of a combination of metformin and glyburide wherein the starting daily dosage is 250 mg metformin and 1.25 mg glyburide, with a maximum daily metformin dosage of 750 mg, where the glyburide has a particle size distribution so that at most 10% of the particles of glyburide are less than ~~[[2]]~~ 11  $\mu\text{m}$  and at most 10% of the particles of glyburide are greater than ~~[[60]]~~ 46  $\mu\text{m}$ .

Claim 59. (Currently Amended) A method for first line treatment of type 2 diabetes, in a drug naïve human patient~~[[,]]~~ who has had no previous oral hyperglycemic treatment or has had no oral hyperglycemic treatment for 2 months, which comprises administering to a drug naïve human patient in need of treatment, as first line therapy, a therapeutically effective low dose of a combination of metformin and glyburide, with a maximum daily metformin dosage of 750 mg, where the glyburide has a particle size distribution so that at most 10% of the particles of the glyburide are less than ~~[[2]]~~ 11  $\mu\text{m}$  and at most 10% of the particles of the glyburide are greater than ~~[[60]]~~ 46  $\mu\text{m}$ , wherein the starting daily dosage is 250 mg metformin and 1.25 mg glyburide once a day or twice a day or 500 mg metformin and 2.5 mg glyburide once a day.

Claim 60. (Currently Amended) A method for first line treatment of type 2 diabetes, in a drug naïve human patient~~[[,]]~~ who has had no previous oral hyperglycemic treatment or has had no oral hyperglycemic treatment for 2 months, which comprises administering to a drug naïve human patient in need of treatment, as first line therapy, a therapeutically effective low dose of a combination of metformin and glyburide, with a maximum daily metformin dosage of 750 mg, where the glyburide has a particle size distribution so that at most 10% of the particles of glyburide

are less than  $[[2]]$  11  $\mu\text{m}$  and at most 10% of the particles of the glyburide are greater than  $[[60]]$  46  $\mu\text{m}$ , wherein the starting daily dosage is 500 mg metformin and 5 mg glyburide.

Claims 61 to 70. (Cancelled).

Claim 71. (Currently Amended) A method for lowering blood glucose in a hyperglycemic human patient which comprises administering to a drug naïve human patient ~~in need of treatment, who has had no previous oral hyperglycemic treatment or has had no oral hyperglycemic treatment for 2 months~~, as first line therapy, a therapeutically effective amount of a low dose of a combination of metformin and glyburide, where the glyburide has a particle size distribution so that at most 10% of the particles of the glyburide are less than  $[[2]]$  11  $\mu\text{m}$  and at most 10% of the particles of the glyburide are greater than  $[[60]]$  46  $\mu\text{m}$ , wherein the metformin in said low dose combination is administered in a daily dosage ~~in an amount within the range from about 160 mg to of at most about 750 mg[[.]]~~ and the glyburide in said low dose combination is administered in a daily dosage in an amount within the range from about 0.5 to about 15 mg.

Claim 72. (Currently Amended) A method for decreasing insulin resistance, decreasing hemoglobinA<sub>1c</sub>, increasing post-prandial insulin levels or decreasing post-prandial glucose excursion, individually or in any combination, in a human patient, which comprises administering to a drug naïve human patient ~~in need of treatment, who has had no previous oral hyperglycemic treatment or has had no oral hyperglycemic treatment for 2 months~~, as first line therapy, a therapeutically effective amount of a low dose of a combination of metformin and glyburide, where the glyburide has a particle size distribution so that at most 10% of the particles of the glyburide are less than  $[[2]]$  11  $\mu\text{m}$  and at most 10% of the particles of the glyburide are greater than  $[[60]]$  46  $\mu\text{m}$ , wherein the metformin in said low dose combination is administered in a daily dosage ~~in an amount within the range from about 160 mg to of at most about 750 mg[[.]]~~ and the glyburide in said low dose combination is administered in a daily dosage in an amount within the range from about 0.5 to about 15 mg.

Claim 73. (Currently Amended) A method for first line treatment of type 2 diabetes, in a drug naïve human patient[[.]] who has had no previous oral hyperglycemic treatment or has had no oral hyperglycemic treatment for 2 months, which comprises administering to a drug naïve human patient in need of treatment, as first line therapy, a therapeutically effective low dose of a combination of metformin and glyburide, with a maximum daily metformin dosage of 750 mg, where the glyburide has a particle size distribution so that at most 10% of the particles of the glyburide are less than [[2]] 11  $\mu\text{m}$  and at most 10% of the particles of the glyburide are greater than [[60]] 46  $\mu\text{m}$ , wherein the glyburide bioavailability is comparable to the glyburide bioavailability obtained with a separate administration of metformin and glyburide.

Claim 74. (Cancelled).

Claim 75. (Previously Presented) The method as defined in Claim 73 where at most 10% of the particles of the glyburide are less than 3  $\mu\text{m}$  and at most 10% of the particles of the glyburide are greater than 40  $\mu\text{m}$ .

Claim 76. (Currently Amended) The method as defined in Claim 73 where at most [[25]] 10% of the particles of the glyburide are less than [[11]] 2  $\mu\text{m}$  and at most [[25]] 10% of the particles are greater than [[46]] 60  $\mu\text{m}$ .

Claim 77. (Previously Presented) The method as defined in Claim 73 wherein 50% of the glyburide particles are less than 23  $\mu\text{m}$ .

Claim 78. (Previously Presented) The method as defined in Claim 73 wherein the glyburide has a particle size distribution of about 25% undersize value not more than 6  $\mu\text{m}$ , about 50% undersize value 7 to 10  $\mu\text{m}$  and about 75% undersize value not more than 23  $\mu\text{m}$ .

Claim 79. (Previously Presented) The method as defined in Claim 73 wherein the starting daily dosage is 250 mg metformin/1.25 mg glyburide or 500 mg metformin/2.5 mg glyburide.